Supplementary Information

Anatomically Distinct Dopamine Release during Anticipation and Experience of Peak Emotion to Music

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SI Guide

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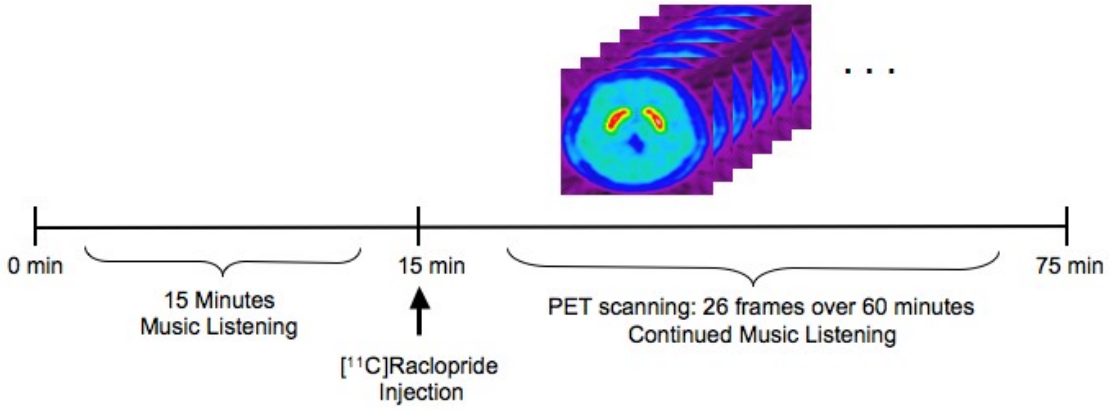

Figure S1: Acquisition of PET scans over two sessions

Each subject participated in two [^{11}C]raclopride PET scans over two days, at approximately the same time of day to control for diurnal variations in dopamine function. Women completed the PET scan between the 10th and14th days of their menstrual cycles to ensure consistency in hormonal levels across participants. Physiological measurements were obtained continuously throughout both PET scanning sessions. PET scans were obtained with a CTI/ Siemens ECAT-HR+ tomograph (CTI PET Systems, Inc., Knoxville, TN), with lead septa removed, operated in three-dimensional mode. Subjects listened to their pleasurable music during one scan and neutral music during the other scan. The scan order was counterbalanced between participants. A catheter was inserted into the antecubital vein for tracer injection. At this point, participants listened to 15 minutes of music to allow for release of dopamine before the radioligand was injected. A transmission scan was acquired using a ^{68}Ge source for the purpose of attenuation correction. After 15 minutes, approximately 10 mCi of [^{11}C]raclopride was injected as a bolus over one minute and emission data were acquired for 60 minutes in 26 time frames of progressively longer duration while participants continued listening to music. After hearing each musical selection participants were asked: (1) how many chills they experienced; (2) rate the intensity of

each chill on a 10-point scale; and (3) rate the overall degree of pleasure they felt in response to the musical excerpt on a 10-point scale.

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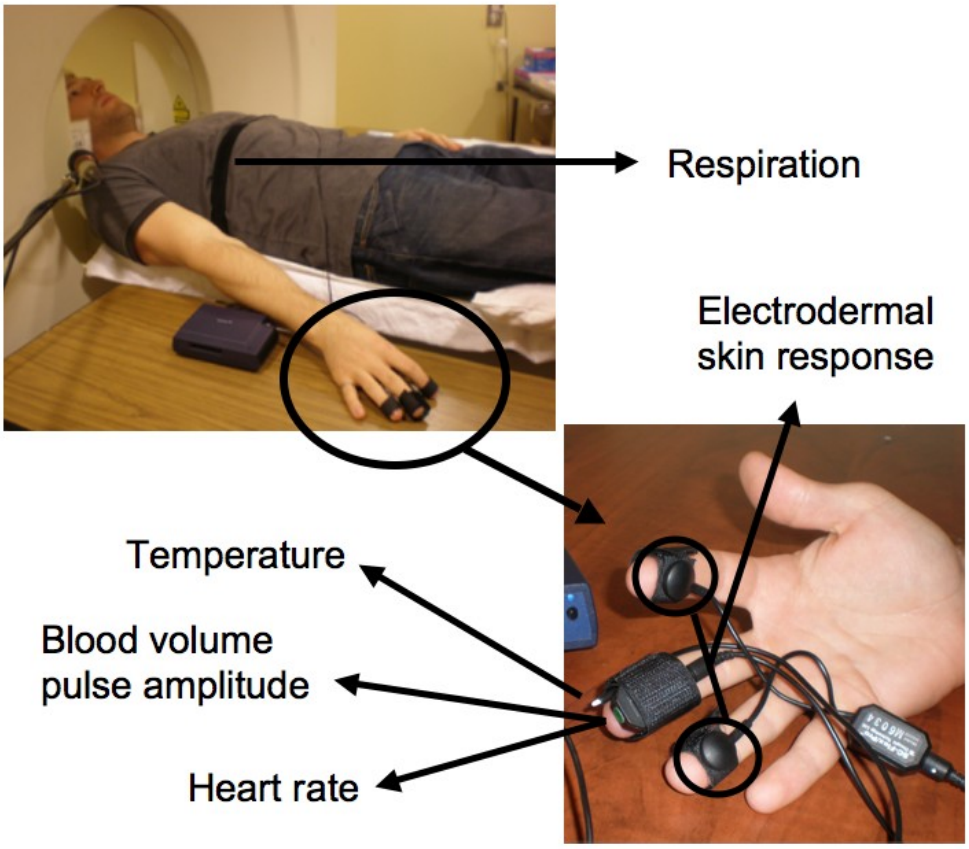

Figure S2. Measures of autonomic nervous system activity during PET scanning

Participants were fitted with psychophysiological equipment to record heart rate, respiration rate, electrodermal activity or galvanic skin response (GSR), blood volume pulse (BVP) amplitude, and body temperature. These sensors consisted of 11mm Ag/AgCl dry electrodes placed on the ring and middle fingers for recording electrodermal activity and secured with Velcro straps, a photoplethysmograph sensor placed on the middle finger for recording heart rate and BVP amplitude also secured with Velcro straps, and a digital thermometer inserted inside the BVP attachment strap on the index finger for recording peripheral skin surface temperature. A Hall effect respiration sensor was placed around the diaphragm to record respiratory rate. Physiological data were collected with the Procom Infinity biofeedback system by Thought Technology (Montreal, Canada). A 5-minute silent period was implemented to provide a baseline from which to examine changes in physiological responses due to music listening.

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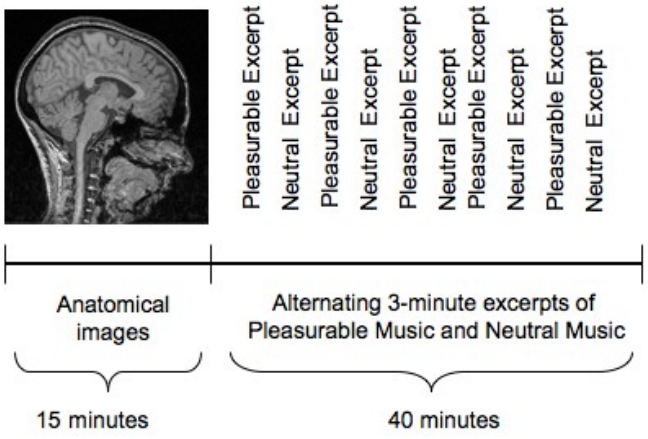

Figure S3. fMRI scans acquired over one session

Functional MRI scans were acquired on a 3 Tesla Siemens TIM Trio scanner using a 1-chanel quadrature coil one to three weeks after completing the PET scan sessions.

A high-resolution T1-weighted anatomical scan was obtained for each participant (voxel size = 1 mm^3) and $T2^*$-weighted echo-planar images of BOLD signal were acquired (35 slices interleaved, 64 × 64 matrix, voxel size = 4 mm^3) aligned with Sylvian fissure and covering the whole brain (TE = 30 ms, TR = 2.1 s). Cardiac gating was used to synchronize image acquisition to a constant phase of the cardiac cycle. High-fidelity headphones were used (MR confon GmbH, 39118 Magdeburg, Germany), containing electrodynamic transducers for a broad, flat frequency response and construction-grade Peltor earmuffs for passive damping of gradient noise. A paradigm similar to the PET scanning was adopted, where individuals listened to their self-selected pleasurable excerpts and other individuals' excerpts which they considered neutral. Participants were also asked to rate the degree of pleasure they were experiencing to the music in real-time (1 = Neutral, 2 = Low-Pleasure, 3 = High-Pleasure) using three separate buttons on an MR-compatible 4-button input device. They were required to hold down the appropriate button as long as they were experiencing the respective degree of pleasure, and press a fourth button when they were experiencing a chill. Individuals were always holding down one button, to ensure that neural activity involved in button pressing and anticipation of button presses were equally distributed. Five 3-minute excerpts of PM

and five 3-minute excerpts of the NM were played in an alternating sequence during a 40-minute run, with a 1-minute break in between excerpts to reduce carry-over effects. To ensure that peak pleasurable responses were maximized, the three minutes that were played in the fMRI scanner were carefully selected according to the following criteria: (1) each selection included the peak pleasure segment (i.e., chills); (2) peak pleasure was placed towards the end of the clips to ensure sufficient "build-up time"; and (3) participants were asked to select the three minutes themselves to ensure that the most subjectively pleasurable minutes were used for this section.

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Psychophysiological Measurement	NM Condition	PM Condition	Welch T-statistic	Correlation with Intensity of Chills
Δ Heart Rate	14.15 (8.09)	17.10 (6.07)	4.04*	r = .34*
Δ Respiration	16.59 (4.93)	20.68 (4.88)	18.14**	r = .31*
Δ Skin Conductance	-.33 (.24)	-.21 (.35)	3.98*	r = .40**
Δ Temperature	-.40 (2.06)	-1.40 (.99)	9.63*	r = -.31*
Δ BVP Amplitude	1.57 (1.62)	-.12 (1.67)	23.63**	r = -.38*

Table S1: Autonomic nervous system activity measurements during PET scanning

Emotional arousal was assessed by measuring changes in heart rate (beats per minute), respiration rate (breaths per minute), skin conductance (microsiemens) peripheral skin temperature (degrees Celsius), and blood volume pulse (BVP) amplitude (reflectance). Mean values during neutral music (NM) and pleasurable music (PM) conditions subtracted from baseline recordings obtained during pre-listening resting phase are reported. Welch's t-tests revealed significant differences between PM and NM scan conditions on all measures. More importantly, within the pleasurable condition, the intensity of chills experienced across excerpts was correlated with the degree of autonomic nervous system arousal: increases in heart rate, respiration, and skin conductance and decreases in temperature and BVP amplitude. (*p<.05, **p<.01)

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Region	Peak MNI Coordinates			t-value	Cluster size (mm^3)	BP change % (SD)
	x	y	z			
Ant. R Caudate	10	19	-2	6.13	868	10.1 (12.4)
R Caudate	12	6	15	4.45	733	7.9 (5.2)
L Caudate	-13	11	7	5.32	896	6.4 (3.5)
R Putamen	26	-2	0	6.99	4426	7.4 (4.2)
L Putamen	-29	-12	-8	6.34	2952	6.6 (8.4)
R NAcc	14	10	-10	4.89	1267	9.2 (8.3)
L NAcc/Ventral Putamen	-21	9	-10	4.94	414	6.5 (14.4)

Table S2: [^{11}C]raclopride binding potential changes between pleasurable and neutral music listening

Significant (*p<.001)* [^{11}C]raclopride binding potential (BP) decreases between pleasurable music (PM) and neutral music (NM) listening conditions in the caudate, putamen, and NAcc. The highest degree of change was found in the anterior right caudate and right NAcc.

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Subjective Reports	BP changes in Right Caudate	BP changes in Right NAcc
Number of Chills	r=.71*	r=.21
Intensity of Chills	r=.26	r=.80*
Degree of Pleasure	r=.19	r=.84**

Table S3: Relationships between [^{11}C]raclopride binding potential changes in striatal regions and subjective reports during music listening

We examined the relationships between subjective reports of pleasure and individual change in [^{11}C]raclopride binding potential (BP) in each of the three clusters that showed significant changes in both BP and BOLD response during anticipation and experience of PER. First the maximum percent change in BP from each significant cluster was extracted for each participant. This value was then plotted against subjective ratings collected during the PET scanning session, namely: (1) the total number of PER reported, (2) the mean intensity of PER, and (3) the mean degree of pleasure. Pearson correlation values were calculated to determine the relationship between BP change and behavioral measures in each of the three significant clusters. The number of chills experienced during the pleasurable music (PM) session was significantly correlated with BP differences in the right caudate, but not the NAcc. The intensity of chills and overall degree of pleasure experienced were most significantly correlated with the right NAcc, but not the caudate. (*p<.05, **p<.01)

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Region	Peak MNI Coordinates			*r* (Excluding Chills)
	x	y	z	
Ant. R Caudate	10	19	-2	.44
R Caudate	12	6	15	.66
L Caudate	-13	11	7	.55*
R Putamen	26	-2	0	.33
L Putamen	-29	-12	-8	.18
R NAcc	14	10	-10	.82**
L NAcc/Ventral Putamen	-21	9	-10	.58

Table S4: Relationships between real-time pleasure ratings during music listening and percent signal change in hemodynamic responses in voxels showing dopamine release.

To determine whether dopamine is involved in pleasure responses independent of the experience of chills, we excluded all chills epochs and compared hemodynamic activity in the NAcc voxel that showed maximum dopamine release during PET scanning with real-time pleasure ratings (i.e., "neutral", "low-pleasure", and "high-pleasure" button-presses) during fMRI scanning. The mean BOLD percent signal change was extracted for each of the three conditions, and a regression analysis was performed to assess whether a change in hemodynamic response can predict pleasure state. To examine whether NAcc was uniquely related to pleasure responses, percent BOLD signal change was extracted for the peak voxels from all other clusters that showed significant dopamine release during PET scanning. A step-wise multiple regression was performed to determine the ability of the signal change in each cluster to predict pleasure state (*p* value was set at .01).

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Regression analyses were performed to examine how well changes in percent BOLD signal change relative to the mean for each voxel showing significant dopamine release could predict real-time pleasure states reported during music listening. The "chills" epochs were not included in this analysis. The results showed that signal changes in bilateral NAcc and caudate clusters could each account for some of the variability in subjective ratings when considered individually (represented by *r* in the table). However, when all clusters were considered in a stepwise multiple regression, signal change in the right NAcc was the single best predictor of increases in subjective ratings, further accounting for much of the variability in the other clusters, particularly that of the right caudate and left NAcc. Signal change in the left caudate could still account for some of the variability in the pleasure ratings not accounted for by right NAcc, since this region was also significant in the multiple regression when thresholds were lowered to $p<.05$. (** $p<.001$, *$p<.05$)

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